APPENDIX I

CURRENTLY PENDING CLAIMS

1. (Twice amended) A method for purifying plasmid DNA suitable for pharmaceutical use from bacterial cells on a large scale, the method comprising the following steps:

a) contacting bacterial cells which together comprise at least about 100 milligrams of the plasmid DNA with a lysis solution, thereby forming a lysis mixture;

b) flowing the lysis mixture through a first static mixer to obtain a lysed cell solution;

c) contacting the lysed cell solution with a precipitation solution;

d) flowing the lysed cell solution and the precipitation solution through a second static mixer, thereby forming a precipitation mixture;

e) centrifuging the precipitation mixture, thereby forming a pellet and a clarified solution comprising the plasmid DNA; and

f) neutralizing either the precipitation mixture prior to the centrifugation of step (e) or the clarified solution following the centrifugation of step (e);

g) contacting the clarified solution with a positively charged ion exchange chromatography resin, wherein the plasmid DNA is eluted from the ion exchange chromatography resin with a saline step or continuous gradient; thereby producing a solution of plasmid DNA of sufficient purity and quantity for pharmaceutical use, wherein the solution comprises at least about 100 mg of the plasmid DNA.

2. The method of claim 1, further comprising the step of RNase digestion.

3. The method of claim 1, wherein the lysis solution contains alkali.

4. The method of claim 1, wherein the precipitation solution contains potassium acetate.

5. The method of claim 1, wherein the neutralizing step precedes the step of centrifuging the precipitation mixture.

6. The method of claim 1, wherein the linear velocity of the lysis mixture through the first static mixer is between about 0.38 to 2.3 feet per second and the first static mixer has an outer diameter in the range of from about 3/16" inch to about 2 inches.

7. The method of claim 6, wherein the first static mixer has 24 elements.

8. The method of claim 6, wherein the first static mixer is a laminar flow static mixer.

9. The method of claim 1, wherein the linear velocity of the precipitation mixture through the second static mixer is between 0.38 to 2.3 feet per second and the second static mixer has an outer diameter in the range of from about 3/16 inch to about 2 inches.

10. The method of claim 9, wherein the second static mixer is a laminar flow static mixer.

11. The method of claim 9, wherein the second static mixer has 24 elements.

12. The method of claim 1, wherein steps (a) and (b) are carried out simultaneously.

13. The method of claim 1, wherein steps (c) and (d) are carried out simultaneously.

14. The method of claim 1, wherein steps (a), (b), (c), and (d) are carried out simultaneously.

15. The method of claim 1, wherein steps (a), (b), (c), (d) and (e) are carried out simultaneously.

16. The method of claim 1, wherein steps (a), (b), (c), (d) (e) and (f) are carried out simultaneously.

17. The method of claim 16, wherein the method is automated.

18. (Amended) The method of claim 1, further comprising filtering the clarified solution through an ultrafiltration unit comprising a gel layer before contacting the clarified solution with the positively charged ion exchange resin.

19. The method of claim 18, wherein the ultrafiltration unit comprises a membrane having a molecular weight cutoff of from about 50K to about 500K daltons.

20. The method of claim 1, further comprising ultrafiltration of the plasmid DNA using tangential flow ultrafiltration with an open channel device, in the presence of a gel layer.

21. A method for purifying plasmid DNA suitable for pharmaceutical use from bacterial cells on a large scale, the method comprising the following steps:

a) contacting bacterial cells which together comprise at least about 100 milligrams of the plasmid DNA with a lysis solution, thereby forming a lysis mixture;

b) flowing the lysis mixture through a first static mixer to obtain a lysed cell solution;

c) contacting the lysed cell solution with a precipitation solution;

d) flowing the lysed cell solution and the precipitation solution through a second static mixer, thereby forming a precipitation mixture;

e) centrifuging the precipitation mixture, thereby forming a pellet and a clarified solution comprising the plasmid DNA; and

f) neutralizing either the precipitation mixture prior to the centrifugation of step (e) or the clarified solution following the centrifugation of step (e);

g) contacting the clarified solution with a positively charged ion exchange chromatography resin, wherein the plasmid DNA is eluted from the ion exchange chromatography resin with a saline step or continuous gradient; and

h) filtering the clarified solution of step (f) through an ultrafiltration unit comprising a gel layer either before or after contacting the clarified solution with the positively charged ion exchange resin of step (g), thereby producing a solution of plasmid DNA of sufficient purity and quantity for pharmaceutical use, wherein the solution comprises at least about 100 mg of the plasmid DNA.